AMENDMENTS TO THE SPECIFICATION:

Please amend the specification as follows:

At page 5, replace the paragraph beginning on line 1 with the following paragraph:

In a first embodiment, the immunoglobulins of the invention are obtainable in prokaryotic cells, especially in E.coli cells by a process comprising the steps of :

a) cloning in a Bluecript vector of a DNA or cDNA sequence coding for the V_{HH} domain of an immunoglobulin devoid of light chain obtainable for instance from lymphocytes of Camelids,
b) recovering the cloned fragment after amplification using a 5' primer containing an Xho site and a 3' primer containing the Spe site having the following sequence TC TTA ACT AGT GAG GAG ACG GTG ACC TG (SEQ ID NO:51),
c) cloning the recovered fragment in phase in the immuno PBS vector after digestion of the vector with Xho and Spe restriction enzymes,
d) transforming host cells, especially E.coli by transfection with the recombinant immuno PBS vector of step c,
e) recovering the expression product of the V_{HH} coding sequence, for instance by using antibodies raised against the dromadary V_{HH} domain.

At page 11, replace the paragraph beginning on line 1 with the following paragraph:

G G S V Q T G G S L R L S C E I S G L T F D (SEQ ID NO:1)
G G S V Q T G G S L R L S C A V S G F S F S (SEQ ID NO:2)
G G S E Q G G G S L R L S C A I S G Y T Y G (SEQ ID NO:3)
G G S V Q P G G S L T L S C T V S G A T Y S (SEQ ID NO:4)
G G S V Q A G G S L R L S C T G S G F P Y S (SEQ ID NO:5)
G G S V Q A G G S L R L S C V A G F G T S (SEQ ID NO:6)
G G S V Q A G G S L R L S C V S F S P S S (SEQ ID NO:7)
for the framework 4 domain

W G Q G T Q V T V S S (SEQ ID NO:8)

W G Q G T L V T V S S (SEQ ID NO:9)

W G Q G A Q V T V S S (SEQ ID NO:10)

W G Q G T Q V T A S S (SEQ ID NO:11)

R G Q G T Q V T V S L (SEQ ID NO:12)

for the CDR3 domain

A L Q P G G Y C G Y G X - - - - - - - - - - - C L (SEQ ID NO:62)

V S L M D R I S Q H - - - - - - - - - - - - - G C (SEQ ID NO:63)

V P A H L G P G A I L D L K K Y - - - - - - K Y (SEQ ID NO:64)

F C Y S T A G D G G S G E - - - - - - - - - - M Y (SEQ ID NO:65)

E L S G G S C E L P L L F - - - - - - - - - - D Y (SEQ ID NO:66)

D W K Y W T C G A Q T G G Y F - - - - - - - - G Q (SEQ ID NO:67)

R L T E M G A C D A R W A T L A T R T F A Y N Y (SEQ ID NO:68)

Q K K D R T R W A E P R E W - - - - - - - - - N N (SEQ ID NO:69)

G S R F S S P V G S T S R L E S - S D Y - - N Y (SEQ ID NO:70)

A D P S I Y Y S I L X I E Y - - - - - - - - - K Y (SEQ ID NO:71)

D S P C Y M P T M P A P P I R D S F G W - - D D (SEQ ID NO:72)

T S S F Y W Y C T T A P Y - - - - - - - - - - N V (SEQ ID NO:73)

T E I E W Y G C N L R T T F - - - - - - - - - T R (SEQ ID NO:74)

N Q L A G G W Y L D P N Y W L S V G A Y - - A I (SEQ ID NO:75)

R L T E M G A C D A R W A T L A T R T F A Y N Y (SEQ ID NO:76)

D G W T R K E G G I G L P W S V Q C E D G Y N Y (SEQ ID NO:77)

D S Y P C H L L - - - - - - - - - - - - - - - D V (SEQ ID NO:78)

V E Y P I A D M C S - - - - - - - - - - - - - R Y (SEQ ID NO:79)

At page 12, replace the paragraph beginning on line 7 with the following paragraph:

According to a particular embodiment of the invention the constant region of the immunoglobulins comprises C_H2 and C_H3 domains comprising an amino-acid sequence selected from the following :

for the C_H2 domain:

APELLGGPTVFIFPPKPKDVLSITLTP (SEQ ID NO:31)

APELPGGPSVFVFPTKPKDVLSISGRP (SEQ ID NO:32)

APELPGGPSVFVFPPKPKDVLSISGRP (SEQ ID NO:33)

APELLGGPSVFIFPPKPKDVLSISGRP (SEQ ID NO:34)

for the C_H3 domain:

GQTREPQVYTLA (SEQ ID NO:35)

GQTREPQVYTLAPXRLEL (SEQ ID NO:36)

GQPREPQVYTLPPSRDEL (SEQ ID NO:109)

GQPREPQVYTLPPSREEM (SEQ ID NO:110)

GQPREPQVYTLPPSQEEM (SEQ ID NO:111)

At page 12, replace the paragraph beginning on line 31 with the following paragraph:

Particular sequences of hinge region of the immunoglobulins of the invention are the following.

GTNEVCKCPKCP (SEQ ID NO:37)

or,

EPKIPQPQPKPQPQPQPQPKPQPKPEPECTCPKCP (SEQ ID NO:38)

At page 16, replace the paragraph beginning on line 31 with the following paragraph:

The invention also concerns nucleotide sequences coding for all or part of a protein which amino-acid sequence comprises a peptide sequence selected from the following :

G G S V Q T G G S L R L S C E I S G L T F D (SEQ ID NO:1)

G G S V Q T G G S L R L S C A V S G F S F S (SEQ ID NO:2)

At page 17, replace the paragraph beginning on line 1 with the following paragraph:

G G S E Q G G G S L R L S C A I S G Y T Y G (SEQ ID NO:3)

G G S V Q P G G S L T L S C T V S G A T Y S (SEQ ID NO:4)

G G S V Q A G G S L R L S C T G S G F P Y S (SEQ ID NO:5)

G G S V Q A G G S L R L S C V A G F G T S (SEQ ID NO:6)

G G S V Q A G G S L R L S C V S F S P S S (SEQ ID NO:7)

W G Q G T Q V T V S S (SEQ ID NO:8)

W G Q G T L V T V S S (SEQ ID NO:9)

W G Q G A Q V T V S S (SEQ ID NO:10)

W G Q G T Q V T A S S (SEQ ID NO:11)

R G Q G T Q V T V S L (SEQ ID NO:12)

A L Q P G G Y C G Y G X - - - - - - - - - - - C L (SEQ ID NO:62)

V S L M D R I S Q H - - - - - - - - - - - - - G C (SEQ ID NO:63)

V P A $_H$ L G P G A I L D L K K Y - - - - - - - K Y (SEQ ID NO:64)

F C Y S T A G D G G S G E - - - - - - - - - - M Y (SEQ ID NO:65)

E L S G G S C E L P L L F - - - - - - - - - - D Y (SEQ ID NO:66)

D W K Y W T C G A Q T G G Y F - - - - - - - - G Q (SEQ ID NO:67)

R L T E M G A C D A R W A T L A T R T F A Y N Y (SEQ ID NO:68)

Q K K D R T R W A E P R E W - - - - - - - - - N N (SEQ ID NO:69)

G S R F S S P V G S T S R L E S - S D Y - - N Y (SEQ ID NO:70)

A D P S I Y Y S I L X I E Y - - - - - - - - - K Y (SEQ ID NO:71)

D S P C Y M P T M P A P P I R D S F G W - - D D (SEQ ID NO:72)

T S S F Y W Y C T T A P Y - - - - - - - - - - N V (SEQ ID NO:73)

T E I E W Y G C N L R T T F - - - - - - - - - T R (SEQ ID NO:74)

N Q L A G G W Y L D P N Y W L S V G A Y - - A I (SEQ ID NO:75)

R L T E M G A C D A R W A T L A T R T F A Y N Y (SEQ ID NO:76)

D G W T R K E G G I G L P W S V Q C E D G Y N Y (SEQ ID NO:77)

D S Y P C H L L - - - - - - - - - - - - - - - D V (SEQ ID NO:78)

V E Y P I A D M C S - - - - - - - - - - - - - R Y (SEQ ID NO:79)

APELLGGPSVFVFPPKPKDVLSISGXPK (SEQ ID NO:39)

APELPGGPSVFVFPTKPKDVLSISGRPK (SEQ ID NO:40)

APELPGGPSVFVFPPKPKDVLSISGRPK (SEQ ID NO:41)

APELLGGPSVFIFPPKPKDVLSISGRPK (SEQ ID NO:42)

GQTREPQVYTLAPXRLEL (SEQ ID NO:36)

GQPREPQVYTLPPSRDEL (SEQ ID NO:109)

GQPREPQVYTLPPSREEM (SEQ ID NO:110)

At page 18, replace the paragraph beginning on line 1 with the following paragraph:

GQPREPQVYTLPPSQEEM (SEQ ID NO:111)

VTVSSGTNEVCKCPKCPAPELPGGPSVFVFP (SEQ ID NO:43)

or,

VTVSSEPKIPQPQPKPQPQPQPQPKPQPKPEPECTCPKCPAPELLGGPSVFIFP (SEQIDNO:44)

GTNEVCKCPKCP (SEQ ID NO:37)

APELPGGPSVFVFP (SEQ ID NO:45)

EPKIPQPQPKPQPQPQPQPKPQPKPEPECTCPKCP (SEQ ID NO:38)

APELLGGPSVFIFP (SEQ ID NO:46)

At page 20, replace the paragraph beginning on line 14 with the following paragraph (double underlining has been used to denote underline in original text):

In a particular example, the following 3' primer in which a KpnI site has been constructed and which corresponds to amino-acids 313 to 319 (CGC CAT CAA GGT AAC AGT TGA) (SEQ ID NO:47) is used in conjunction with mouse V_{HH} primers described by Sestry et al and containing a Xho site

AG GTC CAG CTG CTC GAG TCT GG (SEQ ID NO:48)

AG CTC CAG CTG CTC GAG TCT GG (SEQ ID NO:49)

AG GTC CAG CTT **CTC GAG** TCT GG (SEQ ID NO:50)

XhoI site

At page 22, replace the paragraph beginning on line 22 and bridging page 23 with the following paragraph (double underlining has been used to denote underline in original text):

The clones can be expressed in several types of expression vectors. As an example using a commercially available vector Immuno PBS (Huse et al : Science (1989) 246, 1275), clones produced in Bluescript ® according to the above described procedure, are recovered by PCR using the same XhoI containing 5' primer and a new 3' primer, corresponding to residues 113-103 in the framework of the immunoglobulins, in which an Spe site has been constructed : TC TTA ACT AGT GAG GAG ACG GTG ACC TG (SEQ ID NO:51). This procedure allows the cloning of the V_{HH} in the Xho/Spe site of the Immuno PBS vector. However, the 3' end of the gene is not in phase with the identification "tag" and the stop codon of the vector. To achieve this, the construct is cut with Spe and the 4 base overhangs are filled in, using the Klenow fragment after which the vector is religated. A further refinement consists in replacing the marker ("tag") with a poly histidine so that metal purification of the cloned V_{HH} can be performed. To achieve this a Spe/EcoRI double stranded oligo-nucleotide coding for 6 histidines and a termination codon is first constructed by synthesis of both strands followed by heating and annealing :

CTA GTG CAC CAC CAT CAC CAT CAC TAA* TAG* (SEQ ID NO:52)

AC GTG GTG GTA GTG GTA GTG ATT ATC TTA A (SEQ ID NO:53)

At page 37, replace the paragraph beginning on line 29 with the following paragraph:

Figure 7: Alignment [~~Alignement~~] of 17 V_{HH} DNA sequences of Camel heavy chain immunoglobulins (SEQ ID NO:108)

At page 49, replace the paragraph beginning on line 9 with the following paragraph (double underlining has been used to denote underline in original text):

The clones can be expressed in several types of expression vectors. As an example using a commercially available vector Immuno PBS (Huse et al : Science (1989) 246, 1275), clones produced in Bluescript ® according to the above described procedure, have been recovered by PCR using the same XhoI containing 5' primer and a new 3' primer, corresponding to residues 113-103 in the framework of the immunoglobulins, in which an Spe site has been constructed : TC TTA ACT AGT GAG GAG ACG GTG ACC TG (SEQ ID NO:51). This procedure allowed the cloning of the V_{HH} in the Xho/Spe site of the Immuno PBS vector. However, the 3' end of the gene was not in phase with the identification "tag" and the stop codon of the vector. To achieve this, the construct was cut with Spe and the 4 base overhangs were filled in, using the Klenow fragment after which the vector was religated.

Replace Tables 1-5 at pages 51-55 with attached amended Tables 1-5 on replacement pages 51-55a.

AMENDMENTS TO THE DRAWINGS:

Subject to the approval of the Examiner, Applicants request that Fig. 7A be amended to include SEQ ID NOs along side of each sequence listed in that figure. The requested changes are indicated in red on the attached copy of the originally filed drawing.

Formal drawings, including the amended Figure 7A, are filed concurrently with this Amendment in response to a Notice to File Missing Parts.